QUALITY CONTROL OF INFUSIONS IN PATIENT-SPECIFIC PREPARATIONS FOR ONCOLOGICAL TREATMENT

Lars M. H. Reinders1,2,3, Jacqueline Bruckmann1, Martin D. Klassen1, Claudia vom Eyser1, Martin Jaeger2, Torsten C. Schmidt2, Thorsten Teutenberg1, Jochen Tuerk1
1) Institut für Energie- und Umwelttechnik e. V. (IUTA, Institute of Energy and Environmental Technology), Bliesheimer Straße 58-60, 47229 Duisburg, Germany, teutenberg@iuta.de
2) Hochschule Niederrhein (University of Applied Sciences), Ramanstraße 49, 47655 Krefeld, Germany
3) University Duisburg-Essen, Faculty of Chemistry, Instrumental Analytical Chemistry, Universitätsstraße 5, 45141 Essen, Germany

Motivation

• Within the area of cancer treatment, the therapy regimen is adapted to the patient.
  – Type and dose of the drug are adjusted to the individual needs of the patient.
• Patient individual application solutions are not analyzed.
  – No quality assurance cause a risk of errors.
• Sources of error: stability-, mixing-problems, underdosing and overdosing, as well as drug counterfeiting and deliberate dilutions.
• Incorrectly dosed preparations can lead to increased side effects or to ineffectiveness.
• To improve quality assurance, we compared chromatography coupled to UV-detection versus a method based on a combined Raman and UV detection system (Raman-UV).

Take home message

• Additional quality assurance can improve the accuracy for patient-specific application solutions.
  – 3.2% incorrect dosages (n=126).
• Advantages of Raman-UV
  – Identification of formulation substances and generics.
  – Good distinguishability of monoclonal antibodies.
• Advantages of HPLC-UV
  – Separation of formulation substances is possible.
  – Robust results with less knowledge about the sample.

Steps in preparation

1.) Production of patient-specific applications
2.) Gravimetric analysis
3.) Determination of density
4.) HPLC-UV and Raman-UV

Results and discussion

Cytotoxic agents

• Analysis of 126 patient specific application bags, measured as triplicate.
• Only the active ingredients were known but not the brand.
• Unknown influences of formulation substances.
• The deviation shall not exceed 10%.
  – HPLC-UV: 4 outlier (3.2%).
  – Raman-UV: 24 outlier (19%).
• The marked sample in figure 1 provides a recovery of 9% compared to 97% by HPLC-UV.
  – Different Raman-Spectra.

Monoclonal antibodies

• HPLC-UV analysis of monoclonal antibodies faces several challenges.
  – Nearly the same UV-spectra (Figure 3A).
  – Difficult to separate with common reversed phase chromatography.
  – Analysis time of several minutes.
  – Very robust quantification is possible.
• Monoclonal antibodies differ significantly in their Raman spectra (Figure 3B).
  – Opportunity of identity testing.
  – Formulation substances can lead to interferences.
  – Quantification via UV, as the Raman signals are very weak.
  – Identification and quantification in approximately 90 seconds.

Acknowledgement

We thank B&W TEK for providing the Raman-UV spectrometer and especially Dr. Sara Seiffert for her support and fruitful discussions. We would also like to thank Mr. Pérennec for his help in data export.